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Psychotherapeutic and Adjunctive Pharmacologic Approaches to Treating Posttraumatic Stress Disorder

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ABSTRACT

Posttraumatic stress disorder (PTSD) is a potentially disabling illness that affects millions of people worldwide and can be very difficult to treat, especially the sleep disturbances often associated with this disorder. Successful treatment focuses on psychotherapy, and medications may be useful adjuncts. This article gives examples of successful therapeutic approaches and adjunctive medication use in PTSD.

INTRODUCTION

Posttraumatic stress disorder (PTSD) is characterized by three symptom clusters, including re-experiencing aspects of the trauma, avoidance of reminders of the trauma, and hyperarousal symptoms upon reminders of the trauma. According to the National Comorbidity Survey Replication study,[1] approximately seven percent of adult Americans will meet the criteria for PTSD at some point in their lives. Of the patients who were symptomatic at the time of the study, approximately one third were considered to have severe symptoms, one third moderate, and one third mild.[2]

Severe symptoms were defined as a 12-month suicide attempt with

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serious lethality intent, work disability or substantial limitation, or any disorder that resulted in 30 or more days out of role in the year. Moderate cases were defined by suicide gesture, plan, or ideation, at least moderate work limitation due to a mental or substance disorder, or any disorder with at least moderate role impairment in two or more domains of the Sheehan Disability Scale, which assesses disability in work role performance, household maintenance, social life, and intimate relationships. All other cases were classified as mild.[2]

Complex PTSD is characterized by all of the symptoms associated with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (DSM-IV-TR) definition of PTSD but also more pronounced problems with emotional regulation, self-image, preoccupation with the relationship to the perpetrator (e.g., preoccupied with revenge fantasies), and interpersonal and occupational relationships, including repeated search for a rescuer. See Table 1 for DSM-IV-TR diagnostic criteria for PTSD.

The diagnosis and treatment of PTSD in children provides its own special challenges. Children are apt to display symptoms of PTSD in ways that are different from adults, but common presentations include repetitive play and nightmares. Children who are traumatized are at particular risk for lasting neurobiological changes, including impairments in the corpus callosum, left neocortex, hippocampus, and amygdala.[3] Depending on the circumstances, child trauma survivors may or may not have a chance to develop appropriate object relations and a schema of the world being safe. This predisposes them to a host of comorbid axis I and II disorders, as well as PTSD subsequent to traumas later in life (Table 2).[4]

With regard to treating children with PTSD, evidence is even more sparse, although there is some evidence in favor of trauma-focused

TABLE 1. Diagnostic criteria for 309.81 posttraumatic stress disorder

A. The person has been exposed to a traumatic event in which both of the following were present:

1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
2. The person's response involved intense fear, helplessness, or horror. Note: In children, this may be expressed instead by disorganized or agitated behavior.

B. The traumatic event is persistently reexperienced in one (or more) of the following ways:

1. Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
2. Recurrent distressing dreams of the event. Note: In children, there may be frightening dreams without recognizable content.
3. Acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated). Note: In young children, trauma-specific reenactment may occur.
4. Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
5. Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

1. Efforts to avoid thoughts, feelings, or conversations associated with the trauma
2. Efforts to avoid activities, places, or people that arouse recollections of the trauma
3. Inability to recall an important aspect of the trauma
4. Markedly diminished interest or participation in significant activities
5. Feeling of detachment or estrangement from others
6. Restricted range of affect (e.g., unable to have loving feelings)
7. Sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:

1. Difficulty falling or staying asleep
2. Irritability or outbursts of anger
3. Difficulty concentrating
4. Hypervigilance
5. Exaggerated startle response

E. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month.

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if:

Acute: if duration of symptoms is less than three months
Chronic: if duration of symptoms is six months or more

Specify if:

With Delayed Onset: if onset of symptoms is at least six months after the stressor

TABLE 2. Complex PTSD

Repeated and prolonged exposure to trauma in childhood leads to pervasive and chronic symptoms that may be better described by the concept of complex PTSD as set forth by Herman.[57]

Symptoms include all of those associated with the DSM-IV-TR definition of PTSD but also more pronounced problems with emotional regulation, self-image, preoccupation with the relationship to the perpetrator (e.g., preoccupied with revenge fantasies), and interpersonal and occupational relationships, including repeated search for a rescuer.

Both cognitive processing therapy and Prolonged Exposure therapy can be equally effective for patients with complex PTSD.[58]

cognitive-behavioral therapy (CBT) and eye movement desensitization and reprocessing, as well as play therapy.[5,6]

The sleep disturbances associated with PTSD are some of the most disabling and difficult-to-treat aspects of the disorder. In addition to the insomnia and nightmares that are part of the criteria for diagnosis, patients can develop anxiety over going to sleep or fear of going back to sleep after waking.[7] Such individuals may condition themselves to stay awake as a way to avoid the anxiety induced by their trauma-related nightmares.[8] According to Wittmann,[9] about 50 percent of PTSD dreams are replications of traumatic events, and thus they do not necessarily have stereotypical content.

Singareddy and Balon note that REM-related abnormalities of various sorts are often found on polysomnographic studies of patients with PTSD, but the findings are not consistent across the studies they reviewed.[10] Spoormaker and Montgomery note that the sleep disturbances themselves are a core feature of PTSD and in fact predispose one to PTSD.[11] They also cite the relatively high correlation of periodic limb movements and/or sleep disordered breathing in patients with PTSD as evidence for disturbed sleep requiring specific attention. They note that "with disturbed sleep any (critical) event will be more difficult to process and more likely to result in emotional complaints, and an extremely critical event will therefore be more likely to result in PTSD…" They also note that polysomnographic studies of PTSD patients are prone to be misleading as patients tend to view the sleep lab as a "safe" place and therefore are less likely to have nightmares there. A recent meta-analysis of polysomnographic studies showed that patients with PTSD had more stage 1 sleep, less slow wave sleep, and greater REM density than those without PTSD.[12]

TREATING PTSD THAT INCLUDES ASSOCIATED SLEEP PROBLEMS

Building trust. All forms of treatment share a common element of building a trusting relationship between patient and physician. This is especially important for the patient with PTSD because his or her worldview has been disrupted by trauma(s). This may be further complicated in military populations exposed to combat related traumas. Surveys of soldiers in the field and returning home have found a reluctance to use behavioral health resources. This hesitation is often related to how seeking help would be viewed by commanders and peers. Some of these views may stay with the individual even after separating from the military.[14,15]

"Sleep hygiene" advice can be a place to start with trust-building. Patients who have been traumatized have such a sense of having lost control in their lives, having a sleep hygiene program they can take control of may have additional psychological benefits aside from the sleep quality issues, which may in and of themselves make a tremendous difference.

A book we have found to be a useful resource for our patients is by Breus,[16] who reviews the importance of getting regular exercise, avoiding alcohol, nicotine, and caffeine in the evening, and having a quiet, darkened room in which to sleep; he also discusses the television controversy, which is whether or not to have a television in the bedroom. It includes a sleep diary, a four-week "sleep boot camp" self-help exercise, and additional resources for patients.

Case 1. Mrs. C was a 40-year-old wife of a retired Air Force major who had an extensive history of physical, sexual, and emotional abuse as a child. She also had a number of medical problems stemming from her history of abuse and was never able to get a good night's sleep secondary to nightmares and chronic pain. She reported lying awake for hours at night, unable to get to sleep and becoming very frustrated and angry.

Mrs. C was willing to participate in a sleep study after several sessions of rapport-building with her psychiatrist. She had a number of trepidations about the study initially, but during the course of the study it was discovered that she had moderate to severe sleep apnea and was fitted with a constant positive airway pressure (CPAP) device. She reported nonadherence with the device after several more weeks, stating "I feel like I'm suffocating." After ensuring there was no technical issue with the machine, 12 sessions of desensitization therapy were completed, and Mrs. C was ultimately able to use it on a regular basis, resulting in a decrease of her pain symptoms as well as reduction of depression and anxiety.

Case 2. Miss A was a 28-year-old college sophomore at a local university. She presented to the college mental health service with complaints of depression and

anxiety. A thorough evaluation reveals a long history of PTSD stemming from severe physical, emotional, and sexual abuse by her stepfather from the ages of 4 to 15, at which point she ran away from home and has been on her own ever since. Symptoms included initial insomnia, taking at least two hours to get to sleep, and with multiple awakenings during sleep. She does not recall the content of her dreams, but reports difficulty getting back to sleep after awakening from a nightmare.

Miss A was tried on a number of pharmacotherapeutic options for her insomnia and PTSD, including several selective serotonin reuptake inhibitors (SSRIs), two tricyclics, three benzodiazpines, two non-benzodiazepine hypnotics, and several atypical antipsychotics at various times over the course of her two years in treatment, to no avail, developing side effects that limited her ability to tolerate medications soon after initiating them. Although agreeing to psychotherapeutic approaches at various times, she remained resistant to all forms of therapy, demonstrated by failing to attend sessions consistently for psychodynamic approaches and not adhering with homework for CBT-based approaches. Upon exploration of her difficulties in getting well, it was revealed that she did not at her core believe she would ever be able to get well. It was only after thoroughly exploring this belief that she began to adhere with homework assignments and give up her overreliance on medications to address her symptoms.

Psychotherapy. Psychotherapy is the mainstay of treatment for PTSD, although insomnia is still a frequent complaint after successful treatment of other symptoms.[38] Two psychotherapy approaches designed to specifically address the nightmares associated with PTSD are imagery rehearsal therapy and lucid dreaming therapy.

Imagery rehearsal therapy (IRT). Developed by Krakow and colleagues,[39] IRT is a brief (three session) manualized treatment specifically for nightmares, and may have a positive effect on daytime symptoms of PTSD as well. In this form of therapy, nightmares are seen as a learned habit, and patients are taught positive imagery techniques, and attempt to "re-write" and practice the nightmares using the new "script." IRT has reportedly been used successfully to treat nightmares associated with both sexual assault trauma[40] and combat trauma.[41] The study cited on sexual assault[40] trauma involved 168 women in New Mexico; 88 were randomized to receive treatment over three sessions and 80 were assigned to a control situation. Using an intent-to-treat analysis, the investigators found that there were significant improvements in the sleep function in the treatment group, with additional benefits for daytime symptoms as well. Krakow and Moore wrote a case series of 11 Army soldiers deployed to Iraq with therapy provided over four sessions by Moore while in Iraq. Seven of the 11 showed marked improvements, which were sustained or continued to improve at nine-month follow-up.

Case 6. Mr. G is a 49-year-old sales executive who developed PTSD after being mugged. He suffered frequent recurrent nightmares of the incident, often with even worse outcomes than the incident itself. He underwent imagery rehearsal training in which he rewrote his nightmares with more positive endings and rehearsed them frequently during the day. Eventually, he no longer experienced the original nightmare, although he still remained somewhat symptomatic during the day.

Lucid dreaming therapy (LDT). This is a technique that involves training the patient to realize he or she is dreaming when a nightmare occurs, and possibly even alter the nightmare itself to result in lessened anxiety overall.[42] Randomized, controlled trials are necessary to fully evaluate lucid dreaming as a therapeutic technique.[43] A study by Spoormaker and van den Bout[44] of 23 nightmare sufferers, eight randomized to a single two-hour LDT individual session, eight randomized to a single two-hour group LDT session, and seven wait-list controls revealed no difference in the individual versus group approaches in terms of efficacy in reducing nightmares, and both were more effective than wait list.[44] Patients did not show significant changes in sleep quality or PTSD symptom severity at 12-week follow-up.

In the Spoormaker and van den Bout study,[44] the single session of LDT consisted of exposure, mastery, and lucidity exercises, although they note the lucidity exercises *per se* did not seem to be necessary for reduction in nightmares.[44] One may thus conclude that the success of treatment had more to do with the exposure and mastery components; however, further research is needed.

Case 3. Mr. F is a 48-year-old local business man who suffered PTSD after a motor vehicle accident. He underwent training in LDT. He rehearsed alternative endings to his recurrent dream of the accident, and was ultimately able to implement them during his dreams.

Differential diagnosis. Sleep disturbances can potentially arise from many underlying disorders, and a consideration of the differential is crucial in developing an effective treatment plan with one's patient. Eiser presents a thoughtful discussion of the subject in his recent review.[13] Considerations include nightmare disorder, which may persist through adulthood, sleep terrors, somnambulism, nocturnal seizures, which may manifest as stereotyped recurrent nightmares arising from a temporal lobe focus, REM sleep behavior disorder, obstructive sleep apnea, and hypnogogic/hypnopompic hallucinations associated with narcolepsy. Eiser mentions that these may all have different pathophysiologic manifestations of nightmares, with those nightmares occurring in association with PTSD occurring both within and outside of the context of REM sleep (especially

Stage 2).[13] Issues related to sleep hygiene, circadian rhythm disturbance, or insufficient sleep may also increase nightmares.[13]

TREATING PTSD THAT INCLUDES ENTIRE CLUSTER OF PTSD SYMPTOMS

A recent meta-analysis and systematic review of the literature done by Bisson and colleagues[18] included 38 studies of various forms of psychotherapeutic treatment for PTSD in different patient populations (e.g., including Vietnam veterans only, women only), and concluded that the evidence base is strongest for trauma-focused CBT (including prolonged exposure therapy [PE] and then eye movement desensitization and reprocessing [EMDR]), with no difference in positive response between the two forms of therapy. They did not find as much evidence in support of psychodynamic approaches; however, they note that there were few studies done and that does not necessarily imply lack of efficacy. By their nature, psychodynamic approaches are difficult to administer in a uniform way and this makes systematic study difficult.

Cognitive behavioral therapy (CBT). Perhaps the best known of the manualized therapies, CBT was developed by A. Beck and explicated by J. Beck,[19] and seeks to help the patient understand and change the way he or she thinks about the world and thus change his or her mood. Therapy has a specific, narrow focus and takes place over 12 to 16 sessions with the idea that if one problem can be mastered, the skills learned can be generalized to other problems. Studies have shown that trauma-focused CBT (e.g., CPT, prolonged exposure [PE], and variants) is superior to a generalized form of CBT (e.g., relaxation training) when treating patients with PTSD,[20,21] and therefore discussion will focus on the major forms of trauma-focused CBT. A thorough discussion of the evidence for various forms of trauma-focused CBT is provided in the review by Bisson and Andrew.[21]

Cognitive processing therapy (CPT). Developed by Resick and colleagues,[22] CPT is a manualized therapy that focuses on getting a patient past "stuck points" and processing the impact of the traumatic event on the patient. Patients who are very uncomfortable discussing the traumatic material may find this of benefit as the focus is on the impact to the patient (i.e., their beliefs as to why it happened and how it has changed the way they see themselves and the world around them). Several studies have shown the efficacy of this approach, including a wait-list controlled trial done with 54 men and six women with combat-related trauma in an intention-to-treat analysis. At the conclusion of the study, 40 percent of patients no longer met criteria for PTSD, and 50 percent had "a reliable change in symptoms from their pretreatment assessment."[23] In a study of 71 women with at least one episode of childhood sexual abuse, only seven percent of women who underwent CPT met criteria for PTSD at the end of the study, versus 74 percent of a minimal-attention control, and improvements in function were sustained at one-year follow-up.[24] None of the women in this study had a worsening of symptoms.

Case 4. Miss E was a 26-year-old transfer student from Nigeria at a local university who presented to the local college mental health service with severe nightmares, ruminations, and hyperarousal symptoms, which were interrupting her college education, following an ethnically motivated gang rape several years ago. She underwent a course of 12 sessions of CPT with improvement of all symptoms, with therapy focused on "stuck points" revolving around self-blame for the rape.

Prolonged exposure (PE) therapy. Developed by Foa,[25] PE is a manualized therapy designed to lessen the threat of the trauma to the patient. This is done in a series of 12 to 16 sessions where the patient re-examines the traumatic event multiple times until the fear response is lessened to a manageable level, or ideally, extinguished.

A randomized controlled trial of 277 female veterans and seven female active duty service members found that exposure therapy was superior to present-centered therapy and that those in the exposure condition were more likely to no longer meet criteria for PTSD and to achieve complete remission.[26]

One hundred and seventy-one women with chronic PTSD were randomly assigned to a course of PE with cognitive restructuring or a wait-list control. Investigators found no difference between treatment conditions (i.e., no benefit to the additional cognitive restructuring component), but also found that patients of therapists with minimal experience administering CBT did just as well as those of CBT experts.[27]

In a separate study of 171 women with chronic PTSD, patients were assigned to cognitive processing therapy, PE therapy, or a minimal attention control.[28] No significant difference was found between the two treatment groups, although each had an over 25-percent dropout rate, compared with 15 precent of the control group. CPT seemed to be slightly more effective than PE for improving some measures of guilt.[28]

Case 5. Staff sergeant (SSgt) B was a 45-year-old active duty service member who had served three tours of duty in Iraq. Prior to deployment, he had no significant mental health history. Since his return from the first tour, he had trouble sleeping, and his wife reported that he frequently kicked and punched in his sleep, and she was sleeping in a separate bed because of this. SSgt B reported extensive flashbacks to, ruminations of, and nightmares of his time in Iraq and a particular mission in which he was confronted with the gruesome remains of an individual who had accidentally detonated a bomb he was making.

SSgt B engaged in a course of PE therapy in which he initially related

the story of a particular incident, recorded it, and reviewed the tape repeatedly between sessions. In each session, he would review the incident with his therapist and examined the different aspects of his thought processes and emotions as they emerged. Over the course of 14 sessions, his PTSD Checklist (PCL, a 17-item self-report measure of PTSD severity with scores ranging from 17 to 85)[29] scores were reduced from a high of 70 to a final score of 20, where it remained two years after initial treatment.

SSgt B related in a subsequent interview, "My body was back home, but my mind was still in Iraq. I was looking forward to another deployment just because I felt more comfortable there, less out of place. Now I can look forward to deployment to continue working on our overall mission, and not my personal demons."

Eye movement desensitization and reprocessing (EMDR) therapy. EMDR was developed by Shapiro,[30] and involves reviewing the worst aspect of the trauma with the therapist leading the patient in repetitive horizontal eye movements, and the patient repeating particular coping statements. EMDR takes place over 1 to 4 sessions, and thus is more efficient timewise than other forms of therapy. The precise movement was initially postulated by Shapiro to specifically interrupt the neural pathways involved in memory retrieval and allow the patient to more appropriately reintegrate the memories, although other repetitive movements have been found to be useful as well.[20]

Case 6. Airman D is a 24-year-old female active duty service member who developed PTSD after a motor vehicle accident. She was unable to drive for several months after the initial trauma because of a paralyzing fear of having another accident. She was also plagued with ruminations over the incident and nightmares. She was referred to a community provider who specialized in EMDR and after a four-session course in which she repeatedly reflected on aspects of her accident while guided in horizontal eye movements by her therapist. She was able to drive again, although she still felt twinges of anxiety when getting behind the wheel. She no longer had nightmares and did not ruminate over the incident.

Stress inoculation training (SIT). SIT is another form of CBT, which was developed for the management of anxiety symptoms. It includes an education component and a variety of coping skills, including muscle relaxation, assertiveness training, thought stopping, and other techniques. It has been successfully used to treat rape survivors,[31] motor vehicle accident survivors,[32] and to help prevent PTSD.[33] Meichenbaum provides a comprehensive review of the technique and evidence.[34]

Psychodynamic psychotherapy. *Psychodynamic psychotherapy* is a collective term for several types of therapies, including brief and long-term orientations. Psychodynamic therapies are not manualized but rather allow the patient to guide therapy to some extent. The approach can best be conceptualized by Freud's seminal paper, "Remembering, Repeating and Working Through."[35] It stresses the importance of unconscious material, repression, defense mechanisms, and the impact of a person's life experiences on their present world view and symptom formation.

In psychodynamic psychotherapy, unconscious conflicts are brought to conscious awareness, and the patient-psychiatrist relationship serves as a model for understanding the patient's relationships outside therapy. Brief psychodynamic psychotherapy generally takes place over 12 to 16 sessions, and revolves around a single focus. Long-term psychodynamic psychotherapy ideally occurs over a minimum of 40 sessions, generally once or twice weekly, and examines the various patterns in the patient's life and seeks to make the unconscious tendencies conscious so that destructive cycles can be broken. Psychoanalysis generally occurs 3 to 5 times weekly over years, examining multiple facets of a patient's development and psyche in order to achieve lasting change and character development. Brom and colleagues[36] conducted a randomized, controlled trial of 112 patients with PTSD randomly assigned to brief psychodynamic psychotherapy, trauma desensitization, or hypnotherapy, and found clinically meaningful improvements with all three forms. Eiser[37] describes several psychodynamic explorations of the meaning of nightmares in the larger context of PTSD and an individual's character structure.[13] Psychodynamic psychotherapy may produce change that continues after therapy ends.[37]

Psychodynamic psychotherapy may also be useful for those patients who cannot tolerate CBT, PE, or EMDR, or who wish to gain a deeper understanding into their motivations and character.[37] Brief and group interpersonal approaches have been reported to be useful in treating PTSD, and it may be particularly useful for those with complex PTSD.[37] Schottenbauer notes that psychodynamic psychotherapy may work more slowly than other treatments but studies imply that change continues after therapy ends.[37] Schottenbauer[37] also provides a helpful review of various developmental issues and their implications for psychotherapy.

Case 1, continued. After her adjustment to using her CPAP on a regular basis, Mrs. C was able to engage in brief psychodynamic psychotherapy over 20 sessions with a marked reduction in the quality and quantity of nightmares and an improvement in her relationship with her husband. She is currently contemplating re-engaging in longer-term therapy to address her residual symptoms of PTSD and remains medication-free by her choice.

POWER STRUGGLES WITHIN THE THERAPEUTIC RELATIONSHIP

Patients with PTSD have a strong need to feel in control of something because their illness makes them feel so out of control. Often, this need permeates the therapeutic relationship and results in a conscious or unconscious

TABLE 3. Classes of medications potentially associated with nightmares[59]

ASSOCIATION

Beta Blockers
Atenolol, bisopropol, labetalol, oxprenolol, propranolol
SSRIs
Fluoxetine, escitalopram, nefazodone, paroxetine
Agents Affecting Serotonin and Norepinephrine
Risperidone, venlafaxine
Dopamine Agonists
Amantadine, levodopa, ropinirole, selegiline
Amphetamine-like Agents
Bethanidine, fenfluramine, phenmetrazine
GABA agonists
gamma-hydroxy butyrate, triazolam, zopiclone
Anti-infectives and immunosuppressives
Fleroxacin, ganciclovir, gusperimus
Antipsychotics
Clozapine
Antihistamine
Chlorpheniramine
ACE Inhibitors
Enalapril, losartan, quinapril
Miscellaneous
Digoxin, naproxen, verapamil

POSSIBLE ASSOCIATION

Cholinergic Agonists
Donepezil, rivastigmine, tacrine
SSRIs
Sertraline
Agents Affecting Serotonin and Norepinephrine
protriptyline
Dopamine Agonists
Bupropion, cabergoline
GABA Agonists
Flunitrazepam, gabapentin, nitrazepam, tiagabine
Anesthetics
Ketamine, midazolam
Anti-infectives and Immunosuppressives
Ciprofloxacin, erythromycin
Anti-epileptic Drugs
Ethosuximide, lamotrigine, valproic acid, zonisamide
Antipsychotics
Chlorpromazine, thiothixene
ACE Inhibitors
Captopril
Miscellaneous
Buprenorphine

nonadherence with therapeutic recommendations. The therapist must work with the patient to ensure adherence. It may also manifest as an overreliance on medications, prescription or nonprescription medication, or a complete refusal to consider medications when they might be warranted. Power struggles may also be a sign of wanting to avoid painful material; when this is detected, it should be processed with the patient as it may end up being a barrier to successful treatment.

Some therapists express concern that having patients talk about their traumatic experiences can do more harm than good; however, a Cochrane review[17] of the subject found insufficient evidence to determine whether psychological treatment is harmful.

USING MEDICATION TO TREAT PTSD

A comprehensive, evidence-based review of primary pharmacologic treatments for PTSD may be found at the VA/DoD website.[18] Their primary recommendations are for SSRIs as first-line treatment, with tricyclic antidepressants and monoamine oxidase inhibitors as second-line treatment. They note insufficient evidence to warrant recommending a mood stabilizer or antipsychotic in treating PTSD, and they recommend against the long-term use of benzodiazepines for core symptoms secondary to poor outcomes. Phenelzine, a monoamine oxidase inhibitor, has been shown to improve sleep quality in PTSD.[45]

The novel antidepressants have shown some efficacy, but as of the date of the VA/DoD consensus guidelines there were insufficient studies to recommend them as primary treatment. A recent Cochrane review of the subject revealed similar conclusions.[17] Paroxetine, sertraline, and fluoxetine have all been approved by the US Food and Drug Administration (FDA) to treat PTSD.[46] In the UK, paroxetine, mirtazapine, amitriptyline, and phenelzine are the preferred agents for use in treating PTSD but only after the patient has expressed a preference for not engaging in psychotherapy first.[47]

Prazosin has been shown to be effective in reducing nightmares in combat veterans,[48] and in clinical practice has been effective in patients with trauma from other sources as well. Doses studied were effective from 10 to 16mg; however, in practice, patients can respond with as little as 2 to 4mg at bedtime.

Benzodiazepines are inexpensive and effective in reducing anxiety overall; however, there has been a paucity of studies in examining their use in PTSD. Those studies that have been done have not shown a benefit

for reducing nightmares, and more importantly, benzodiazepines can increase the chance of PTSD developing when administered to recently traumatized individuals.[46] They can also worsen sleep apnea.[46]

A paucity of studies have been conducted on non-benzodiazepine GABA agonists, but there were positive results in one small study on zolpidem, which Maher notes is also less likely to exacerbate sleep apnea.[46]

Trazodone is a triazolopyridine derivative used as both an antidepressant and a sleep aid. It is inexpensive, but its use can be limited by nasal congestion, dry mouth, blurred vision, and priapism, among others. In a study by Warner,[49] 43 of 72 patients found trazodone to be helpful in reducing nightmare frequency, and 55 found it to be helpful with sleep onset.

Clonidine is an α_2-adrenergic agonist that has been shown to be useful in treating both daytime and nighttime symptoms of PTSD in children and adults with trauma from various sources.[50]

Mirtazapine may be useful for PTSD as it has both anxiolytic and sedative properties. It also may be helpful for obstructive sleep apnea.[46]

Tricyclics are often used as hypnotics; however, there have been insufficient studies to recommend their use in PTSD patients. Side effects and toxicity in overdose warrant caution.[46]

Phenelzine, a monoamine oxidase inhibitor, has been shown to improve sleep quality in PTSD.[45]

Several atypical antipsychotics are well known for their sedative properties and can be useful when other medications have failed, particularly when the patient suffers comorbid bipolar or psychotic illness, or even borderline personality disorder. None of these medications are FDA-approved for use in PTSD, and long-term side effects and cost are detriments. There is some evidence for the use of clozapine, olanzapine, risperidone, and quetiapine in patients with severe symptoms.[51]

RESIDUAL SYMPTOMS

Treatment resistance. PTSD can be very difficult to treat, particularly if there are multiple and/or early traumas, which predispose the patient not only to the neurobiological alterations discussed previously but also to complex PTSD and various dissociative and personality disorders. Another consideration is the patient's thoughts on getting better—is he willing to allow himself to heal or does he have a conscious or subconscious investment in staying ill? Unfortunately, PTSD can be easily malingered,[52] and the clinician must be alert to this possibility whether or not there is obvious secondary gain. Even if the patient is not malingering, he may have some motivation for overreporting his symptoms. If the patient is not improving despite appropriate therapeutic interventions, the clinician may wish to consider referral for psychometric testing, including the Minnesota Multiphasic Personality Inventory (MMPI) if appropriate. One must also question one's original diagnosis and reconsider whether there are additional axis I, II, or III disorders contributing to treatment resistance, including nightmares induced by medication treatments being used for the PTSD itself or another condition (Table 3).[59]

Case 7. Technical Sergeant (TSgt) F is a 48-year-old active duty Air Force member who presented for a Fitness for Duty examination at the request of his commander, who noticed a marked decline in TSgt's work performance over the past three months, approximately one year after his return from Afghanistan. His unit was preparing to be redeployed soon, and TSgt F was not looking forward to going. He was having marital problems, and his wife was threatening to divorce him if he left for deployment again.

"Doc, I just can't sleep at night, and I'm having all these flashbacks about the war." When questioned about his deployment, he stated, "I never actually left Bagram (the major air base in Afghanistan), but I heard stories about what it was like outside the wire. You can't send me back!" Upon further questioning, TSgt F admitted his main reluctance revolved around his marital problems. Arrangements were then made for TSgt F and his wife to attend marital therapy, but as the time for deployment approached, Mrs. F could not reconcile herself with the idea of having her husband gone for another tour. They ultimately divorced.

Serotonin syndrome. Patients with PTSD are often started on an antidepressant, either by a psychiatrist or a primary care provider. Signs and symptoms of mild serotonin syndrome can be mistaken for worsening PTSD, including anxiety, akathisia, and hypervigilance.[53] These can all worsen sleep disturbances associated with PTSD.

Case 8. Mrs. D was started on citalopram for anxiety. After her first dose, her anxiety became noticeably worse. After her second dose, she had a protracted anxiety attack lasting three hours, including symptoms of rapid heartbeat, feeling excessively warm, and shaking "that seemed to go all over my body." She stopped the medication and reported her symptoms at her scheduled follow-up visit.

Chronic pain. Patients with PTSD also often have chronic pain as a consequence of physical abuse, hypersensitivity of their nervous systems (limbic system), somatoform illness, or concurrent anxiety disorder. Primary care physicians or pain specialists may treat them with tramadol, which has a potent serotonergic effect, which may be underappreciated by practitioners. Clinicians should note that there have been several cases of serotonin syndrome reported in the literature in patients with tramadol and SSRIs.[54,55]

CONCLUSION

PTSD is a potentially disabling condition that affects millions worldwide. Successful treatment depends on a strong therapeutic alliance, and medications may be useful adjuncts. Astute clinicians will keep in mind a careful differential diagnosis and potential axis I, II, and III disorders when working with treatment-resistant patients.

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